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Cont'd*

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and wherein all monosubstituted substituents have either an  $\alpha$  or  $\beta$  configuration.

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#### REMARKS

Applicants' representatives thank Examiner Qazi for the telephonic inquiry on September 23, 2002 in the above-referenced application, and have entered the above amendments in reply thereto.

Claims 1-38 are currently pending in this application. Claims 1-9 were cancelled by the Response to Restriction Requirement filed May 9, 2002, and Claims 31-38 are cancelled by this Amendment, therefore, Claims 10-30 are presently under examination. Claims 1, 11 and 19 are amended herein, support for which is found in the specification, therefore no new matter is added to this application.

Claims 1 and 11 are both amended to define the 17-position ring substituent  $>C-R_g$  as  $>C(H)-OH$  only. Further, element e) of Claim 1 recites that the 16-position ring substituents  $R_{h1}$  and  $R_{h2}$  cannot both be H. Element e) of Claim 1 has been reproduced in independent Claims 11 and 19. The definitions of  $R_g$ ,  $R_{h1}$ , and  $R_{h2}$  as amended in Claims 1, 11 and 19 now clearly distinguish these independent claims from the broadest claims of U.S. Patent Application Numbers 09/899,702 (our file 05213-0910) and 09/939,208 (our file 05213-0852), as also amended today.

Further, Claims 1-9, which were cancelled by the Response to Restriction Requirement filed May 9, 2002, and were made the subject of the related application directed to compound claims, Application Serial No. 09/779,331 (our file no. 05213-0731). The claims of

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the present application are directed to a method of inhibiting angiogenesis, therefore, the present application is patentably distinct from the invention described in Application No. 09/779,331, and thus not subject to a double patenting rejection.

Applicants further note that the present Application and Applications Number Applications No. 09/779,331, 09/899,702, and 09/939,208 were commonly owned and/or subject to an obligation to assign to the same entity at the time the inventions were made (35 U.S.C. § 103(c)), thereby precluding an interference proceeding.

Accordingly, Applicants respectfully maintain that Claims 10-30 are patentably distinct and hence allowable, and such action is respectfully requested.

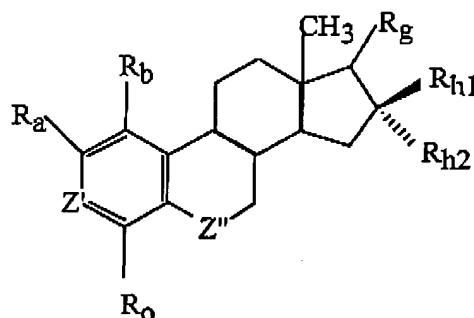
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# VERSION WITH MARKINGS TO SHOW CHANGES MADE

## Amendments in the Claims

In accordance with 37 C.F.R. § 1.12(c), the following version of the rewritten claim shows all the changes made by the foregoing amendment relative to the previous version of that claim.

10. (Twice Amended) A method of inhibiting angiogenesis comprising administering to an endothelial cell an angiogenesis inhibiting amount of a compound of the general formula:



wherein:

- a)  $R_b$  and  $R_o$  are independently -H, -Cl, -Br, -I, -F, -CN, lower alkyl, -OH, -CH<sub>2</sub>-OH, -NH<sub>2</sub>; or N( $R_6$ )( $R_7$ ), wherein  $R_6$  and  $R_7$  are independently hydrogen or an alkyl or branched alkyl with up to 6 carbons;
- b)  $R_a$  is -N<sub>3</sub>, -C≡N, -C≡C-R, -CH=CH-R, -R-CH=CH<sub>2</sub>, -C≡CH, -O-R, -R-R<sub>1</sub>,

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-OC(O)CH<sub>3</sub>, -C(O)H, -NH<sub>2</sub>, -NMe<sub>2</sub>, -NHMe or -O-R-R<sub>1</sub> where R is a straight or branched alkyl with up to 10 carbons or aralkyl, and R<sub>1</sub> is -OH, -NH<sub>2</sub>, -Cl, -Br, -I, -F or CF<sub>3</sub>;

c) Z' is >CH, >COH, or >C-R<sub>2</sub>-OH, where R<sub>2</sub> is an alkyl or branched alkyl with up to 10 carbons or aralkyl;

d) >C-R<sub>g</sub> is [>CH<sub>2</sub>,] >C(H)-OH[, >C=O, >C=N-OH, >C(R<sub>3</sub>)OH, >C=N-OR<sub>3</sub>, >C(H)-NH<sub>2</sub>, >C(H)-NHR<sub>3</sub>, >C(H)-NR<sub>3</sub>R<sub>4</sub>, or >C(H)-C(O)-R<sub>3</sub>, where each R<sub>3</sub> and R<sub>4</sub> is independently an alkyl or branched alkyl with up to 10 carbons or aralkyl];

e) R<sub>h1</sub> and R<sub>h2</sub> are independently H, or a straight or branched chain alkyl, alkenyl or alkynyl with up to 6 carbons that is unsubstituted, or substituted with one or more groups selected from a hetero functionality (O-Y, N-Y<sub>2</sub> or S-Y) where Y is independently selected from H, Me or an alkyl chain up to 6 carbons; a halo functionality (F, Cl, Br or I); an aromatic group optionally substituted with hetero, halo or alkyl; or R<sub>h1</sub> and R<sub>h2</sub> are independently an aromatic group optionally substituted with hetero, halo or alkyl, provided that both R<sub>h1</sub> and R<sub>h2</sub> are not H;

f) Z'' is >CH<sub>2</sub>, >C=O, >C(H)-OH, >C=N-OR<sub>5</sub>, >C(H)-C≡N, or >C(H)-NR<sub>5</sub>R<sub>5</sub>, wherein each R<sub>5</sub> is independently hydrogen, an alkyl or branched alkyl with up to 10 carbons or aralkyl;

and wherein all monosubstituted substituents have either an α or β configuration.

11. (Amended) The method of Claim 10, wherein:

R<sub>b</sub> and R<sub>o</sub> are H,

R<sub>a</sub> is OCH<sub>3</sub>

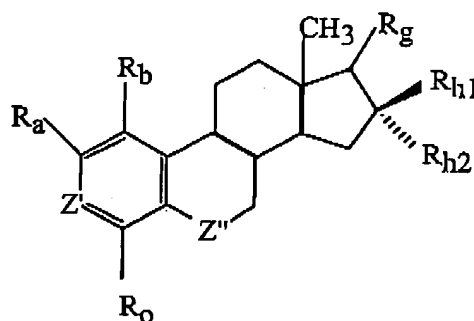
Z' is >C-OH,

[>C-R<sub>g</sub> is >C(H)-β-OH,] and

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$Z''$  is  $>CH_2$ .

19. (Amended) A method of inhibiting angiogenesis comprising administering to an endothelial cell an angiogenesis inhibiting amount of a compound of the general formula:



wherein:

$R_a$  is  $-N_3$ ,  $-C\equiv N$ ,  $-C\equiv C-R$ ,  $-CH=CH-R$ ,  $-R-CH=CH_2$ ,  $-C\equiv CH$ ,  $-O-R$ ,  $-R-R_1$ ,  $-OC(O)CH_3$ ,  $-C(O)H$ ,  $-NH_2$ ,  $-NMe_2$ ,  $-NHMe$ , or  $-O-R-R_1$  where  $R$  is a straight or branched alkyl with up to 10 carbons or aralkyl, and  $R_1$  is  $-OH$ ,  $-NH_2$ ,  $-Cl$ ,  $-Br$ ,  $-I$ ,  $-F$  or  $CF_3$ ; with the proviso that  $R_a$  is not  $OMe$ ;

$R_b$  and  $R_o$  are  $H$ ,

$Z'$  is  $>C-OH$ ,

$>C-R_g$  is  $>C(H)OH$ ,

$[R_{h1}$  and  $R_{h2}$  are  $H$ , and]

$R_{h1}$  and  $R_{h2}$  are independently  $H$ , or a straight or branched chain alkyl, alkenyl or alkynyl with up to 6 carbons that is unsubstituted, or substituted with one or more groups selected from a hetero functionality ( $O-Y$ ,  $N-Y_2$  or  $S-Y$ ) where  $Y$  is independently

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selected from H, Me or an alkyl chain up to 6 carbons; a halo functionality (F, Cl, Br or I); an aromatic group optionally substituted with hetero, halo or alkyl; or  $R_{h1}$  and  $R_{h2}$  are independently an aromatic group optionally substituted with hetero, halo or alkyl, provided that both  $R_{h1}$  and  $R_{h2}$  are not H; and

$Z''$  is  $>CH_2$ ,

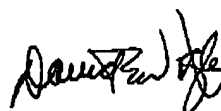
and wherein all monosubstituted substituents have either an  $\alpha$  or  $\beta$  configuration.

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**Conclusion**

In view of the above amendments and remarks, Applicants believe that the claims are now in condition for allowance. Such action is respectfully requested. If there are informalities remaining in the application which may be corrected by Examiner's Amendment, or there are any other issues which can be resolved by telephone interview, a telephone call to the undersigned attorney at (404) 745-2420 is respectfully solicited.

Respectfully submitted,



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Attorney Docket No. 05213-0730 (43170-219693)